REMARKS

Claims 1-4, 6-13, 19-27, 29-35 and 37-39 are in this application. Claim 27 has been amended to delete "non-human"; this was unnecessary as a modifier of insect. None of the amendments made herein constitutes the addition of new matter.

Allowable Subject Matter

Claims 1-4, 6-13, 19-26, 29-35 and 37-39 have been allowed.

The Rejection under 35 U.S.C. 102

Claim 27 has been rejected under 35 U.S.C. 102,(b) as allegedly anticipated by Rong et al. (Science 388: 2013-2018, 2000). Applicant respectfully traverses this rejection.

The Patent Office has taken the position that any insect with a chromosomal segment that could have been inserted by the recited method would read on the instant claim. Rong is said to teach that recombinant Drosophila were made by gene targeting (i.e., homologous recombination).

The transgenic insect of claim 27 is made by the method of transforming an insect comprising exposing replicative tissue of the insect to an element of claim 1 under conditions effective to incorporate the element into the genome thereof and, subsequently or simultaneously therewith, providing conditions suitable to excise said repeats from the genome, and selecting an organism, or tissue therefor, comprising the DNA intended for insertion lacking repeats in at least one orientation, wherein the inverted repeats of the transposable element are repeats from Class II transposable elements. Claim 1 recites the transposable element which comprises 1) **at least four inverted repeats**, forming at least two pairs of opposing pairs of inverted repeats, and 2) DNA for insertion into a host genome (the transgene) located between two pairs of opposing repeats such that excision by a transposase or transposases of said pairs, *in situ*, is effective to be able to leave said DNA integrated into the host genome, **without the presence of said repeats flanking said DNA insertion.**

We refer to the as-filed Specification at page 17 (first two full paragraphs, reproduced below) for a discussion of the sequence of molecular events in the present methods used to create the claimed transgenic insect.

Transposable elements generate a short tandem repeat at the target site when they insert. In the case of piggyBac this target site duplication is TTAA (for most transposons it is of

defined length and sequence, for a few (e.g., P, which is also a Class II transposon) it is just of a defined length). Normally, this duplication (tandem repeat) is then removed when a prior art transposon (transposable element) excises.

However, this duplication/tandem repeat is **not** eliminated when the transposable element of the present invention is used and the inverted repeats have been excised. Accordingly, the final insertion has a unique structure not obtainable with the prior art transposable elements or methods. This is discussed (with reference to the piggyBac system for ease of explanation) in paragraphs [0092] to [0093] of the US publication (the first two full paragraphs on page 17 of the international specification as filed):

> There is no lower limit to the amount of DNA that can be inserted by the overall procedure, after the flanking transposons have been excised. **The initial insertion will retain the target site specificity of the original element**, such as TTAA for piggyBac, with some apparent preference for *(NT)N(NT)TTAA(NT)N(NT)*, which mayaiso be written as WNWTTAAWNW (SEQ ID NO. 20) where "W" denotes A or T. **Precise excision of the elements will resolve this to a duplication of the TTAA, flanking the DNA of interest**, which can be as short as a single nuc1eotide. In the event that zero nucleotides are inserted, only the TTAA duplication remains. The insertion of larger fragments is generally preferred.
>
> A suitable example of a small insertion is a stop codon. Insertional mutagenesis using transposable elements is a well known method for genetic screens of various types. However, interpreting the phenotype may be complicated by the presence of the transposon, with its associated markers, promoters and other elements. A short insertion, such as TTAA or CTAG, which provides a total sequence between the piggyBac ends of TTAATTAATTAA (SEQ ID NO. 1) and TTAACTAGTTAA (SEQ ID NO. 2), respectively, allows the insertion to be resolved to a TTAA duplication with this four base insertion. TTAATTAATTAA (SEQ ID NO. I) and TTAACTAGTTAA (SEQ ID NO. 2), in these examples, provide stop codons in all three frames in both directions. An insert of zero base pairs provides a frame shift and a stop codon in two frames, although one of these is already present in the original TTAA.

In other words, at an insertion site, a duplication of the target sequence is made upon insertion of any transposon. Normally, when the transposon excises, the duplication is deleted. However, the present element is different and once the inverted repeats have been removed, the remaining 'DNA for insertion into a host genome' is now flanked by both the original and the duplicated insertion sites. "The initial insertion will retain the target site specificity of the original element, such as TTAA for piggyBac, ….. Precise excision of the elements will resolve this to a duplication of the TTAA, flanking the DNA of interest…" The DNA of interest "…can be as short as a single nucleotide. In the event that zero nucleotides are inserted, only the TTAA duplication remains. Depending on the class II transposable element used to mediate the

genetic modification of the insect, there will be other duplicated sequences remaining in insects in which the claimed transposable element is inserted and then excised.

Rong does not disclose these molecular events, which will of necessity be embodied in the claimed insect herein. Thus, the instant transgenic insect claimed is genetically distinct from one described in the Rong publication.

Applicant respectfully maintains that the transgenic insect of claim 27 is not anticipated by the cited art. Rong does not disclosure the use of a transposon with at least four inverted repeats and the removal of those inverted repeats. In the present claimed methods, the pairs of inverted repeats are removed, leaving the transgene flanked by tandemly repeated target site sequences created upon insertion of the transposon containing the transgene. Rong does not appear to show this.

In view of the foregoing elucidation of the mechanisms of the present methods leading to the claimed transgenic insect, Applicant maintains that the invention of claim 27 is not anticipated by the cited reference, and the rejection should be withdrawn.

Conclusion

It is submitted that this case is in condition for allowance, and passage to issuance is respectfully requested.

If there are any outstanding issues related to patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time.

This Amendment is accompanied by a Petition for Extension of Time (one month) and payment of the fee of $65.00 required by 37 C.F.R 1.17(a) via the Electronic Filing System. It is believed that no other fees are due and that no further extension of time is necessary. If this is incorrect, however, please deduct the correct fee, and any fee required for any further extension of time, if needed, from Deposit Account 07-1969.

Respectfully submitted,

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